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DETAILED DESCRIPTION

[Detailed Description of the Invention]
[0001]
[Field of the Invention]This invention relates to the cell or the culturing method of an organization which starts the cell and tissue culture art in which it is used for the tissue engineering which is application of cellular structure engineering, gene therapy, etc., and is used for a cell required for restoration of the deficit organization of a human body, etc., or the explantation of an organization, and its device.
[0002]
[Description of the Prior Art]There are the following methods in restoration of a living body's deficit part or an abnormal spot. The 1st [the] is a method for which materials other than living bodies, such as a plastic, metal, and ceramics, are substituted as a restoration means of a deficit part or an abnormal spot. As a substitute, there are ceramics for bones, a stainless steel, polyethylene resin for joints, a vinyl resin for blood vessels, etc. The 2nd has a method of substituting biomechanical materials, such as other animals and other parts. There are the skin etc. in this substitute. The 3rd is the method of transplanting others' organ.
[0003]In the 1st method, the necessity for exchange may arise periodically by wear of materials other than living bodies, such as a plastic, metal, and ceramics, and consumption, or the substance separated by wear etc. may have an adverse effect to a living body. The example of getting an inside blocked is also reported by use of the long period of time [blood vessel] in the blood vessel of the synthetic resin. In the 3rd method, if there is no donor of an organ who should transplant, operation is impossible, and even when it carries out, the problem of the rejection between organs remains.
[0004]For this reason, the repairing method which requires expectation of utilization is a method of assigning the cell and tissue which were produced by cultivating a cell or tissue outside that inside of the body or body in the living body cell to restoration of a defective part. It is reported to many organizations, such as the skin, a cartilage, a bone, a blood vessel, liver, and the pancreas, by the present research that there is the possibility. If the cell and tissue which cultivated a cell or tissue outside a patient's inside of the body and a body from the living body's

cell, and were obtained by the culture are assigned to restoration of defective parts, A rebirth of an organization unreproducible in a body can be performed, moreover, since the organization which used for restoration is an organization with a patient's own gene, there is not no rejection, and chemicals other than a biomechanical material do not necessarily have an adverse effect on a living body, for example like a synthetic resin. An ideal therapy is attained.

[0005]By the way, JP,9-313166,A "cell culture device" is conventionally proposed as this kind of art.In this art, after sterilizing by disassembling and washing each part article for every culture, a device must be assembled again and there is a possibility that it may be polluted by bacteria after sterilization. In order to prevent contamination, after assembling a device, it is possible to perform sterilization treatment, such as autoclave (121 degreeC absolute pressure of 2 atmospheres), but since the pump and the pressure sensor contain many electronic parts, special resin, and oil, they cannot be used on a pollution control. Therefore, a pump and a pressure sensor decompose the part, take out only the circulation space of culture medium, sterilization by medicine is performed, and the danger of saprophytic-bacteria contamination is high [parts], in order that they may sterilize with autoclave and may assemble a pump, a pressure sensor, and a device after that while other parts require time and effort. A pump and a control device tend to be damaged with temperature and humidity, and cultivating using an incubator (culture warehouse) can accommodate no devices in the incubator which has a limitation in capacity. For this reason, in order to let the electric wire for piping, or a power supply and control pass to the through hole of an incubator, where an incubator and the open air are connected, it must finish setting up a device. In order to put a pressure on the whole circuit of culture medium, the whole including parts, such as a pump and piping, must be made into resisting pressure structure, but setting out of a high pressure (for example, 1 or more MPa) is dramatically difficult, if it is going to give high pressure force, the whole must be made into high-withstand-pressure structure, and a cost hike will pose a problem.

[0006]The research which cultivates a body tissue is reported by Harvard Medical School Dr. Shuichi Mizuno etc., applying a pressure as physical irritation conventionally. [MaterialsScienceand Engineering C6301(1998)-306] .When according to this research the culture apparatus is constituted as shown in drawing 26, and each element in this culture apparatus and its function are explained, the pump 400, The role which circulates the culture medium 402, and the role which pressurizes the inside of the culture chamber 404 and gives the cell 406 or tissue hydrostatic pressure are played, for example, the pump for fluid chromatography is used, and the control device for passing constant flow is built in.

[0007]If the back pressure regulator 408 becomes more than the pressure which it is going to give to the cell 406 or tissue, it will open the valve 410, will miss a pressure and will keep the pressure of culture chamber 404 inside constant. The back pressure regulator 408 is chosen and attached according to the pressure which it is going to give to the cell 406.

[0008]The culture chamber 404 constitutes the space which cultivates the cell 406 or tissue, and what planted the cell 406 or tissue in the scaffold 412 which consists of sponge formed by collagen is accommodated in this culture chamber 404. The cell 406 or tissue is increased on the

scaffold 412 which consists of sponge of collagen.
[0009]The pressure sensor 414 detects the pressure in the culture chamber 404, and the pressure monitor 416 displays the detection pressure power of the pressure sensor 414. The pump 400 is controlled by this detection pressure power, and when it becomes excessive [that detection pressure power], it suspends operation of the pump 400.
[0010]The culture medium tub 418 collects the culture medium 402 suitable for the cell 406 or tissue which cultivates, and this culture medium 402 consists of amino acid, sugars, salts, etc., for example. The vent filter 424 prevents contamination by the open air through the open air through the ventilating tube 422 which the culture medium tub 418 made the restricting plug 420 penetrate.
[0011]This culture apparatus is accommodated in the incubator which is a closed space. This incubator is space which forms a comfortable culture atmosphere, and is maintained by a cell, the optimal temperature for an organization, humidity, and gas concentration (oxygen, carbon dioxide). And the culture medium 402 is filled by the pump 400 in the circuit 426, and it circulates through it with it. Oxygen and carbon dioxide pass the vent filter 424, and penetration and the culture medium 402 are maintained at the culture medium 402 by a moderate oxygen density and carbon dioxide gas concentration. If the pressure in the culture chamber 404 will rise gradually if the pump 400 is operated, and it becomes more than the setting pressure of the back pressure regulator 408, Since the pressure of the culture medium 402 declines, the valve 410 closes only a part for the valve 410 of the back pressure regulator 408 to have opened, to have discharged the culture medium 402, and for the culture medium 402 to have discharged. A constant pressure is maintained by repetition of such operation and circulation of a constant rate of culture medium 402 is simultaneously repeated. The cell 406 or tissue is increased receiving such pressure stimulation.
[0012]In this culture apparatus, although a constant pressure is maintainable, rise and fall of a pressure are unrepeatable. Since a pressure buildup is based on the pump 400, if the climbing speed of a pressure is decided by capability of the pump 400 and increases the circulating load of the culture medium 402, a climbing speed will become quick, and a pressure buildup will become slow if the circulating load is set up few. For this reason, when repeating a pressure cycle continuously, in order to drop a pressure, there is a method of installing the bypass passage 432 provided with the bypass valve 428 and the orifice valve (needle valve) 430 in parallel with the back pressure regulator 408 like drawing 27. In this method, although pressure lowering becomes possible, while the time which one cycle takes becomes long, there is a fault that cannot make setting out of a repeating cycle and the circulating load of the culture medium 402 become independent, and regulation of the orifice valve 430 becomes delicate, and the rate of the failure of pressure becomes unstable.
[0013]And after sterilizing by disassembling and washing each part article to the degree of implementation of culture, in order to have to assemble a device, fear of contamination is after sterilization. Although it is possible to perform sterilization treatment, such as autoclave (121 degreeC absolute pressure of 2 atmospheres), for the assembled device for a pollution control,

since many electronic parts, special resin, and oil are contained, the pump and the pressure sensor are impossible. For this reason, under the present circumstances, a pump and a pressure sensor decompose a part, and take out only the circulation space of culture medium, sterilization by medicine is performed, after other portions sterilize with autoclave, they must assemble a pump, a pressure sensor, and a device, and require time and effort, and fear of saprophytic-bacteria contamination is also high [portions].

[0014]Although oxygen to culture medium and incorporation of carbon dioxide are letting the filter pass, since a line is directly from the surrounding atmosphere, there is also fear of contamination. Although this culture apparatus is accommodated in an incubator, it is difficult in capacity to tend to damage a pump unit and a pressure monitor with temperature and humidity, and to accommodate a pump unit and a pressure monitor in an incubator. For this reason, it must finish setting up a device by connecting that inside and exterior with the through hole of an incubator through the tube for piping, or a power supply and the electric wire for control.

[0015]Its danger of saprophytic-bacteria contamination is high while setting out of a pressure requires time and effort, in order to choose and incorporate the back pressure regulator according to a setting pressure, to change setting out of a pressure and to have to exchange a back pressure regulator.

[0016]When changing a pressure cycle, the culture apparatus shown in drawing 27 cannot set up the low-tension side, and though the pressure regulation which is a grade which is the orifice valve 430 is possible, the set-up pressure changes with the circulating flowing quantity of the pump 400.

[0017]

[Problem(s) to be Solved by the Invention]Thus, in the conventional living body's cell, or the culturing method of an organization, the temperature in an incubator (culture warehouse), humidity, carbon dioxide levels, and an oxygen density are set as the optimal conditions, and the cell is cultured in it. In culture by such an incubator, it is superficial (two-dimensional) culture on a petri dish, and the trial of three-dimensional culture has accomplished. And in such a culturing method, the culture medium, the cell, or tissue exposed to the open air tends to be polluted by bacteria, and stable culture is difficult.

[0018]And although a living body's cell is always under physical irritation and those stimuli have affected indirectly the concentration gradient of control of the metabolism of a cell, a cell division cycle, and a living thing stimulus, distribution, etc., It was difficult to realize it stably and setting out and change of the quantity of physical irritation, change, a cycle, etc. were dramatically difficult. And in culture, delicate setting pressure and adjustment are needed, and a culture person's in charge skill is required.

[0019]For this reason, the explantation of the conventional living body cell required time for making it grow up to be a size of the part which should be restored, and normal culture might be spoiled by contamination etc.

[0020]Then, this invention makes it a technical problem to provide the culturing method of the cell or tissue which realized efficient explantation with prevention of contamination, and its

device.
[0021]
[Means for Solving the Problem]While this invention installs a culture position (culture chamber 20) under environment controlled arbitrarily, such as environment imitating a living body, Culture medium (3) is supplied holding a cell (5) or tissue in said culture position, and by cultivating said cell or said tissue in said culture position under ideal environment, while planning a pollution control, said cell or efficient explantation of said organization is realized.
[0022]A cell of this invention or a culturing method of an organization concerning claim 1, A cell (5) or tissue of a living body is held in a specific culture position (culture chamber 20), while setting up said cell or said tissue under environment imitating a living body, culture medium (3) is supplied to said cell or said tissue, and said cell or said tissue is cultivated in said culture position.
[0023]That is, as for an organization required for restoration of some living bodies which suffered a loss, it is ideal to use a cell and tissue of the living body. In order to realize this, it is carrying out explantation of it using a cell and tissue which extracted from a living body. Important things are a pollution control and realizing artificially culturing environment equivalent to a living body, i.e., environment imitating a living body, in this explantation. Then, a cell or explantation of an organization is realized by setting a culture position as environment formed artificially, holding a cell or tissue in this culture position, and supplying culture medium. Here, environment shows survival conditions which include a stimulus of the inside of the body required to maintain the life healthily and the outside of the body on the basis of a living body formed by a cell or tissue. Culture medium includes a nutrient required for growth while maintaining a cell or a life of an organization. In this case, supply of culture medium gives a cell or tissue physical irritation called hydrostatic pressure and a flow, It becomes a cell or tissue receives influence in a concentration gradient of metabolism, a division cycle, and a living thing stimulus, or distribution, the culture is promoted, and, as a result, it is close to inside-of-the-body tissue, and possible to cultivate a cell or tissue which is easy to unite with inside-of-the-body tissue.
[0024]A cell of this invention or a culturing method of an organization concerning claim 2, A cell (5) or tissue of a living body is held in a specific culture position (culture chamber 20), While setting up said cell or said tissue under environment imitating a living body and supplying culture medium to said cell or said tissue continuously or intermittently through a culture circuit (culture circuit unit 4), Continuation, an intermission, or a pressure that changes periodically is applied to said cell or said tissue, and said cell or said tissue is cultivated in said culture position.
[0025]It is as having already described setting out and configuration of a culture position. Culture medium is supplied continuously or intermittently through a culture circuit to a cell or tissue set as a culture position. By supplying culture medium through the external world and a culture circuit separated or intercepted, a supplying form of culture medium can be performed continuously or intermittently, simultaneously a pollution control can be planned. By controlling also about a supplying form of culture medium corresponding to a living body's environment, a

living body can be copied and culture of a cell or tissue can be performed efficiently. And during culture, make a desired pressure act on a cell or tissue, are adding physical irritation, and a gestalt of the pressure, By considering it as continuation, an intermission, or a periodic change, a living body can be copied and physical and mechanical intensity required for living bodies, such as pliability required for a cell or tissue cultivated and endurance, can be given. It will contribute to culture of a cell which is close to an ideal and practical cell corresponding to a living body's part which should be restored, or tissue, i.e., inside-of-the-body tissue, as for this, and is easy to unite with inside-of-the-body tissue, or tissue.

[0026]A cell of this invention or a culturing method of an organization concerning claim 3 is provided with holding mechanism which makes said cell which should be cultured in said culture position, or said tissue hold by floating state or a non-floating state in said culture medium. That is, when it raises culture efficiency that a cell or tissue which should cultivate holds to a static state, a required thing is checked by experiment. Then, a cell or the tissue can realize efficient culture by holding in the state of floating or un-floating in culture medium.

[0027]Hydro-gell which a cell of this invention or a culturing method of an organization concerning claim 4 makes hold said cell or said tissue by a floating state in said culture medium to said holding mechanism, Or while holding said cell or said tissue, a scaffold absorbed by said cell or said tissue with the growth was used. That is, a cell or tissue which should cultivate may be held how and hydro-gell or a scaffold is that example in this case. Hydro-gell is a means to wrap in a cell or tissue which should cultivate and to hold to a floating state, and when culture is completed, it can take out a cell and tissue from the hydro-gell. A scaffold can be constituted from a porous body which consists of protein, and although a cell or tissue cultivated is held on the scaffold, it absorbs the scaffold as nourishment with growth.

[0028]A cell of this invention or a culturing method of an organization concerning claim 5 constituted said culture medium including 1 of various amino acid, sugars, salts, or protein, or 2 or more. That is, what was constituted including two or more substances or all that could use a thing according to a cell or tissue which should cultivate, for example, was chosen from one or these of various amino acid, sugars, or protein can be used for culture medium. When selection of culture medium forms efficient culture, and a quality cell or tissue, they are main elements.

[0029]In addition to a physiological condition of said living body's part, or this physiological condition, said environment where a cell of this invention or a culturing method of an organization concerning claim 6 cultivates said cell or said tissue is set up according to characteristic data for said every living body of age, height, weight, sex, and others. That is, consistenting with the living body is most important for a cell or tissue which uses for restoring some living bodies, and it sets up culturing environment, using the living body's characteristic data as the element.

[0030]A cell of this invention or a culturing method of an organization concerning claim 7 is set up with gas, such as nitrogen in which said environment is supplied through said culture medium, oxygen, or carbon dioxide, temperature, or humidity. Namely, since environment corresponding to a living body is desirable, as the example, environment where a cell or tissue should be

cultivated sets up living body environment, such as setting out of supply of gas, such as nitrogen, oxygen, or carbon dioxide, temperature, or humidity, and controls it in the desired state.
[0031]A cell of this invention or a culturing method of an organization concerning claim 8 sets up arbitrarily said pressure applied to said cell or said tissue according to said cell or said part of said organization. That is, an ideal and practical cell or tissue can be formed by applying a pressure corresponding to a living body's part which should be restored.
[0032]A cell of this invention or a culturing method of an organization concerning claim 9 is characterized by said pressure applied to said cell or said tissue being a pressure which consists of continuation, an intermission, pressures that change periodically, or these combination. That is, by making a pattern of a pressure into continuation, an intermission, or a gestalt that changes periodically, and choosing or combining it, ideal physical irritation can be realized, metabolism of a cell, a concentration gradient of a division cycle and a living thing stimulus, and distribution can be affected, and promotion of culture can be aimed at.
[0033]This invention concerning claim 10 is characterized by a cell or a culture apparatus of an organization comprising the following.
Culture units which are provided with a culture chamber (20) which accommodates a cell (5) or tissue, and supply culture medium (culture circuit unit 4).
A force means which gives said cell or said tissue in said culture chamber a pressure (pressure impression device 16).
A culture medium feeding means to which said culture units are made to supply said culture medium intermittently or continuously (culture medium feed unit 6).

[0034]That is, culture units accommodate a cell or tissue which should cultivate in a culture chamber, and supply the open air, an intercepted cell, or culture medium required for an organization. The open air, an intercepted cell, or tissue is protected from contamination of a biomass etc., and, as a result, grows up to be a quality organization. In addition to physical irritation by hydrostatic pressure by culture medium, and a flow, a desired pressure is given to a cell or tissue by force means. As a result, influence is received in a concentration gradient of metabolism of a cell, a division cycle, and a living thing stimulus, or distribution, and culture of a cell or tissue is promoted. Since a supplying form of a cell or culture medium to an organization is set up arbitrarily and can be supplied intermittently or continuously by a culture medium feeding means, promotion of culture is achieved by physical irritation with a variation. A supplying form of culture medium includes either or both sides of supply which repeats and circulates supply of always new culture medium, and culture medium. Although culture medium can be saved in a gestalt to circulate, probably, in one-way supply, it will be advantageous at a point that a concentration change of culture medium can be prevented.
[0035]A cell of this invention or a culture apparatus of an organization concerning claim 11 was provided with a control means which controls said force means or said culture medium feeding means. Namely, although a force means or a culture medium feeding means is arbitrarily controllable, control of various kinds, such as feedback control and feed-forward control,

programmed control, etc. are possible for it by using a control means of a computer etc. Of course, it is possible to consider human correction control by interruption, and correction controlling is not eliminated.

[0036]A cell of this invention or a culture apparatus of an organization concerning claim 12 sets up arbitrarily said pressure applied to said cell or said tissue according to said cell or said tissue from said force means. How, i.e., a pressure pattern, to apply a pressure can perform more efficient culture by setting up corresponding to a cell or tissue which should cultivate.

[0037]As for a cell of this invention or a culture apparatus of an organization concerning claim 13, said pressure applied to said cell or said tissue from said force means is characterized by a thing which were followed for every intermittence state and fixed time and which is made to fluctuate for every fixed time repeatedly. That is, the pressure pattern can assume all gestalten and can perform culture of a cell or tissue efficiently by the selection.

[0038]A cell of this invention or a culture apparatus of an organization concerning claim 14 is characterized by being disengageable independently from a main part of a culture apparatus in said culture units. Namely, culture units provided with a culture chamber which accommodates a cell or tissue which cultivated, A cell or tissue can be independently moved [main part / of a culture apparatus] with the open air and separated culture units separation and by supposing that it is removable, and a cell or tissue can be protected from contamination by a biomass etc. during movement.

[0039]A cell of this invention or a culture apparatus of an organization concerning claim 15 accommodates said culture units in the open air and an intercepted closed space. That is, closed space is culture spaces, and while setting out of culturing environment by supply of desired gas is attained by being intercepted with the open air, a cell or tissue can be protected from contamination by the open air.

[0040]A cell of this invention or a culture apparatus of an organization concerning claim 16 was provided with a gas-absorption means which can absorb gas, such as nitrogen, oxygen, or carbon dioxide. That is, while supplying gas, such as nitrogen, oxygen, or carbon dioxide, to culture units accommodated in a closed space, by equipping culture units with a gas-absorption means, gas can be given to a cell or tissue and living body environment can be copied by supply and control of gas.

[0041]A cell of this invention or a culture apparatus of an organization concerning claim 17 makes it come to fill up said closed space gas, such as nitrogen, oxygen, or carbon dioxide. That is, living body environment can be copied by making culture spaces formed of a closed space fill up with gas, such as nitrogen, oxygen, or carbon dioxide.

[0042]A cell of this invention or a culture apparatus of an organization concerning claim 18 is provided with a culture medium tub which collects said culture medium which should be supplied to said culture units. That is, in order to supply or circulate culture medium required for culture units, a culture medium supply source is required, and a culture medium tub is the supply source. If a culture medium tub is especially installed in the open air and an intercepted closed space, contamination of saved culture medium can be prevented.

[0043]A cell of this invention or a culture apparatus of an organization concerning claim 19 was provided with a pressure-receiving film pressured from the exterior to said culture chamber. That is, while being able to give an application-of-pressure stimulus in the state where it intercepted with the open air, to a cell or tissue accommodated in a culture chamber by having installed a pressure-receiving film, an application-of-pressure stimulus of a request of a stimulus imitating living body environment, etc. is realizable.
[0044]A cell of this invention or a culture apparatus of an organization concerning claim 20 equipped said culture units with a pressure buffering means. That is, if the pressure regulation is performed by a pressure buffering means when some culture units are pressurized, physical irritation near living body environment can be realized, and promotion of culture of a cell or tissue can be aimed at.
[0045]A cell of this invention or a culture apparatus of an organization concerning claim 21 attaches a pressure chamber to said culture chamber via said pressure-receiving film, makes water pressure, oil pressure, or pneumatic pressure act on this pressure chamber, and applied a pressure to said cell or said tissue in said culture chamber. Namely, as means forming of a pressure, even if it uses any of water pressure, oil pressure, or pneumatic pressure, a desired application-of-pressure stimulus can be realized, and living body environment can be copied with sufficient accuracy.
[0046]A cell of this invention or a culture apparatus of an organization concerning claim 22 provided a liquid-sending chamber in said culture units, and constituted said culture medium feeding means from a liquid-sending device which pressurizes and sends out said culture medium incorporated into this liquid-sending chamber. Namely, although a culture medium feeding means is a means to make culture units supply or circulate through culture medium and the gestalt can assume various kinds of things, For example, a liquid-sending chamber is provided, and if constituted from a liquid-sending device which pressurizes and sends out culture medium incorporated into this liquid-sending chamber, the desired amount of liquid sending can be set up by controlling a pressurizing amount.
[0047]A cell of this invention or a culture apparatus of an organization concerning claim 23 installs a pressure relief valve in said culture units, when a pressure of said culture medium exceeds a constant pressure arbitrarily set as said pressure relief valve, opens said pressure relief valve and drops a pressure of said culture medium. Namely, a thing for which a pressure applied to culture medium is buffered, When exceeding a constant pressure set up to a pressure relief valve arbitrarily [in order to give a cell or tissue an ideal application-of-pressure stimulus it is very important, and / using a pressure relief valve as the way stage / a pressure of culture medium], It can control to an ideal pressure condition, without making culture medium pollute, if a pressure relief valve is opened and a pressure of culture medium is dropped.
[0048]A heating method or a humidification means is installed, said closed space is maintained by a desired temperature or humidity, and a cell of this invention or a culture apparatus of an organization concerning claim 24 is controlled. That is, temperature and humidity of a closed space in which culture units are accommodated can be controlled, and culture spaces

corresponding to living body environment can be formed.
[0049]A cell of this invention or a culture apparatus of an organization concerning claim 25 was provided with a sound generator which gives sound waves, such as an ultrasonic wave, to said culture chamber of said culture units. That is, a living body has received an acoustical stimulus from the external world, and can copy living body environment acoustically by using a sound generator together. When pouring in a cell or tissue which should cultivate to a culture chamber, an ultrasonic wave can be used together and efficient and reliable pouring can be performed.
[0050]A cell of this invention or a culture apparatus of an organization concerning claim 26 is provided with a control means which controls gas concentration supplied to said closed space, and is characterized by things. That is, by controlling gas concentration supplied to a closed space by a control means, living body environment can be copied and a cell or promotion of culture of an organization can be aimed at.
[0051]
[Embodiment of the Invention]Drawing 1 shows the cell of this invention or the culturing method of an organization, and a 1st embodiment of the device.
[0052]The culture apparatus 1 which realizes a cell or the culturing method of an organization is provided with the closed space 2 as those culture spaces, and the culture circuit unit 4 as culture units which supply the culture medium 3 to the cell or tissue which should cultivate is installed in this closed space 2. this culture circuit unit 4 -- the device main frame side and separation -- it can set up removable. This culture circuit unit 4 is provided with the fork road 13 while it is provided with the culture medium tub 9, the culture medium feed unit 6, the culture pressurizer 8, the gas-absorption device 10, and the valve 11, and the valve 15 is formed in this fork road 13. The culture medium 3 is a career which gives the cell which it is going to culture, and tissue nourishment, It is the fluid having contained an essential amino acid, various amino acid, and glucose (sugars), and minerals, such as Na^+ and Ca^{++}, may be added according to the cell and tissue which are going to cultivate, or protein, such as a blood serum, may be included. These devices can prevent contamination with component parts by having sufficient heat resistance, such as a fluoro-resin, PEEK, high-heat-resistance grade polypropylene, silicone, and a stainless steel, and constituting using a resin material without elution of a substance which affects a living body.
[0053]Being able to constitute the valves 11 and 15 from a pinch valve etc., the culture circuit unit 4 serves as an open loop circuit in part by opening both a full admission loop circuit and the valves 11 and 15 by opening a closed loop circuit and the valve 15 by closing the valve 15 and opening the valve 11, and closing the valve 11. The gas-absorption part 41 which replaces the culture circuit unit 4 with the gas-absorption device 10 installed selectively, and is shown with a two-dot chain line, It may have the pressure part 43 shown as a solid line, and they are a portion which makes the culture medium 3 absorb the gas the gas-absorption part 41 was made full [gas] of the closed space 2, and a portion which the pressure part 43 secures liquid sending which is reliable corresponding to the pressurized part of the culture medium 3, and prevents liquid leakage. The tube formed with the elastomeric material etc. which are easy to penetrate

gas, such as CO_2 and O_2 gas, for example can be used for the gas-absorption part 41.

[0054]The culture medium tub 9 is a means for it to be accommodated in the closed space 2 and to collect a cell or the culture medium 3 required for culture of an organization. The culture medium feed unit 6 is a means to supply the culture medium 3 to the culture circuit unit 4, drives the liquid-sending device 12 inserted in the culture circuit unit 4 with the drive 14, and supplies the culture medium 3 of the specified quantity to the culture circuit unit 4. The culture pressurizer 8 is a means to pressurize the cell 5 (drawing 3) or tissue which should cultivate, and is provided with the pressure impression device 16 and the pressure buffer 18. The pressure impression device 16 attaches the pressure vessel 22 to the culture chamber 20 of the culture circuit unit 4, and makes arbitrary pressures act on the culture chamber 20 with the drive 24. In the culture chamber 20, the cell or tissue which should cultivate on the scaffold fabricated from collagen etc. is planted and accommodated, and is isolated from the external world.

[0055]The pressure buffer 18 is a means to buffer the pressure of the culture medium 3 pressurized with the culture pressurizer 8, The pressure relief valve 26 inserted in the culture circuit unit 4 is driven with the drive 28 to the pressure of the culture medium 3 exceeding a predetermined value, maximum pressure is set up, and when the pressure of the culture medium 3 exceeding the maximum pressure acts, a pressure is buffered by missing the culture medium 3. The fluid for application of pressure is poured into the pressure vessel 22 from the liquid injection device 30 for application of pressure put side by side to the culture pressurizer 8.

[0056]The humidity control device 32, the thermostat 34, and gas mixture and a concentration adjustment 36 are installed in this culture apparatus 1, and the humidity, temperature, and gas mixture and concentration of atmosphere are adjusted. It is for the manual operating device 38 performing desired adjustment operation by an administrator, The control device 40 is a means to control the various device of the culture medium feed unit 6, the culture pressurizer 8, the liquid injection device 30 for application of pressure, the humidity control device 32, the thermostat 34, and gas mixture and concentration adjustment 36 grade by the operational input and control program from the manual operating device 38.

[0057]Next, explanation of the cell or the culturing method of an organization using this device will input necessary information, such as a culture condition, by operation of manual operating device 38 grade to the control device 40 as culture preparation. In this case, or necessary information sets what kind of pressure as the culture medium 3, it is, and that setting-out gestalt is pressure inclinations, such as a maximum pressure, minimum pressure, its pressure up, or decompression, an application-of-pressure cycle, a flow of the culture medium 3, culture temperature, culture time, etc. The culture circuit unit 4 chooses whether it is considered as a closed loop, or it is considered as an open loop by switching opening and closing of the valves 11 and 15.

[0058]Next, the scaffolds 7 (drawing 3), such as sponge of collagen, are installed into the culture chamber 20, and the cell 5 (drawing 3) or tissue which should cultivate on this scaffold is planted. The sponge of collagen may be formed by freeze-drying collagen liquid within the culture chamber 20.

[0059]Next, after putting the culture medium 3 of a stipulated amount into the culture medium tub 9 and closing the closed space 2, a driving switch is thrown in and the fluid for application of pressure is supplied to the pressure vessel 22 side by preparation (automatic operation) of culture operation from the liquid injection device 30 for application of pressure.
[0060]If the culture medium feed unit 6 drives, the culture medium 3 will flow into the culture chamber 20 side through the liquid-sending device 12, and the culture medium 3 will be supplied to the cell or tissue which should cultivate. As for the supplying form of this culture medium 3, it is chosen any of continuation, and intermittent and these cycle combination they are.
[0061]The cell or tissue held by the scaffold is accommodated in the culture chamber 20 filled with the culture medium 3, and a pressure is applied to this cell or tissue from the pressure vessel 22. This pressure is based on the pressure pattern set up by culture preparation.
[0062]And when the pressure applied to the culture medium 3 exceeds a setting pressure, the culture medium 3 flows out of the pressure part 43 through the pressure relief valve 26, and pressure regulation is performed.
[0063]By repeating such operation during predetermined culture time, a cell or tissue grows up to be a desired size within the culture chamber 20. When the sponge of collagen is used for the scaffold, the cell or tissue cultivated absorbs the collagen, and a scaffold disappears automatically.
[0064]When hydro-gell is used for holding mechanism, a cell or tissue is accommodated and held by the floating state in the hydro-gell.
[0065]The valve 15 is closed, when the valve 11 is opened and the culture circuit unit 4 is closed-loop-ized, the culture medium 3 circulates through the inside of the culture circuit unit 4, and the culture medium 3 is supplied to the cell [which should be cultured], or tissue side. When the valve 11 is closed, the valve 15 is opened and the culture circuit unit 4 is open-loop-ized, it can be flowed through the culture medium 3 into the fork road 13 side, and can be flowed through it into the liquid injection device 30 68 (drawing 2), i.e., application-of-pressure tank, side for application of pressure, and the always fresh culture medium 3 can be supplied to the cell [which should be cultured], or tissue side.
[0066]And gas, such as nitrogen, oxygen, and carbon dioxide, is absorbed from the inside of the closed space 2 during culture by the culture medium 3 which carries out conduction to the gas-absorption device 10 or the gas-absorption part 41 of the culture circuit unit 4, and gas required for the same gas exchange as a living body is supplied to a cell or tissue through the culture medium 3.
[0067]Thus, the culturing environment imitating a living body is set up, and explantation can be efficiently given to a cell or tissue, without being polluted by the biomass etc. Namely, since the physical irritation by the hydrostatic pressure and the flow of the culture medium 3 is added within the culture chamber 20, influence is received in the concentration gradient of metabolism, a division cycle, and a living thing stimulus, or distribution, and, as for a cell or tissue, culture is promoted. A cell or tissue receives physical irritation according to the application of pressure by the pressure impression device 16, and its application-of-pressure gestalt. As a result, culture of a

cell or tissue is promoted, it is close to tissue in the living body, and inside-of-the-body tissue and the organization which is easy to unite can be cultivated. The cost which resisting pressure structure takes can be reduced by setting up the pressure part 43 selectively.

[0068]Next, drawing 2 shows the concrete embodiment of the culture apparatus 1, and drawing 3 expands and shows the pressure impression device 16 and the pressure buffer 18 of some culture circuit units 4 of the culture apparatus 1, the culture medium feed unit 6, and the culture pressurizer 8. The culture apparatus 1 is the composition that the culture circuit unit 4 is detached and attached, as shown in drawing 4.

[0069]This culture apparatus 1 is provided with the culture warehouse 42 which can be sealed, and opening and closing of the door 270 (drawing 14) are detected by the door switch 44. The culture circuit unit 4 which supplies the culture medium 3 is accommodated in this culture warehouse 42. This culture circuit unit 4 is a removable tube unit which connected the culture medium bag 48 as a culture medium tub which collects the culture medium 3 via the culture chamber 20, the liquid-sending device 12, and the pressure relief valve 26 by the tubes 50A, 50B, 50C, 50D, and 50E. The tubes 50A, 50D, and 50E are the gas-absorption parts 41 (drawing 1), Comprising [and] a ventilating tube which comprised an elastomeric material etc. which can absorb the gas in the culture warehouse 42, the tubes 50B and 50C are the pressure parts 43 (drawing 1), and comprise a resisting pressure tube which bears the pressure of the culture medium 3. And the gas absorption part 52 which makes the tube 50E crooked and absorbs the gas in the culture circuit unit 4 is formed in the tube 50E.

[0070]The culture medium bag 48 is supported by the hook 56 which equips the wall surface of the culture warehouse 42 with the detection switch 54 as a weight detection means, and the capacity of the culture medium 3 in the culture medium bag 48 is detected by the weight with the detection switch 54. When this detection switch 54 detects reduction of the specified weight of the culture medium bag 48, it notifies of that abnormality through a displaying means (display 232), a telephone, etc. through the control device 40. The culture medium discharge part 58 is branched and formed in the tubes 50A and 50E between the gas absorption part 52 and the liquid-sending device 12, and it is opened and closed by the valve 59 for a check. The culture medium 3 which this valve 59 for a check is a means for extracting the culture medium 3 in the culture circuit unit 4, and was extracted from the culture medium discharge part 58, The inspection of pH, concentration, output, an oxygen density, carbon dioxide levels, etc. can be presented [whether it is polluted with substances, such as the denaturation state, i.e., a biomass etc., and].

[0071]The cell 5 which should be cultured is implanted to the scaffold 7 formed by collagen etc., and is accommodated in the culture chamber 20 with the scaffold 7. This culture chamber 20 is constituted by the culture vessel 61, the culture vessel 61 is removably attached to the pressure chamber 60 by the fixing means of two or more bolt 62 grades, and the injection port 63 is formed. This injection port 63 is used in order to implant from the exterior the cell 5 which should be cultured on the scaffold 7 installed in the culture chamber 20 with an injector etc. Other fixing means like a clamping circuit may be used for immobilization of the culture chamber 20. The pressure chamber 60 and the culture vessel 61 are closed by sealants, such as an O ring. The

surface part by the side of the pressure chamber 60 of the culture chamber 20 is blockaded by the pressure-receiving film 64, a closed space is formed, and the application-of-pressure water 65 in the pressure chamber 60 is in contact with the culture chamber 20 via this pressure-receiving film 64.

[0072]The application-of-pressure water (liquid) tub 68 is connected with the pressure chamber 60 through the feed water pipe line 66, the flowing water sensor 70, the pump 80, the bypass valve 82, and the closure valve 84 are formed in the feed water pipe line 66, and the by-pass line 88 which has the orifice 86 in the middle is established in the bypass valve 82. That is, it can be filled up with the application-of-pressure water 65 in the pressure chamber 60 from the application-of-pressure tank 68 by opening the bypass valve 82 and the closure valve 84, and driving the pump 80. Since the application-of-pressure tank 68 is supplemented with the application-of-pressure water 65 through the feed water pipe line 94 by opening and closing the feed water valve 92 according to the water level since the application-of-pressure water level of the application-of-pressure tank 68 is detected by the water level sensor 96, the water level of the application-of-pressure tank 68 can always be held to the optimal water level. The drainage pipe way 98 has branched in the feed water pipe line 66 of the application-of-pressure tank 68, at the time of the end of culture of the cell 5, the sewer valve 100 is opened and the application-of-pressure water 65 is drained.

[0073]The collection pipe way 102 which goes to the application-of-pressure tank 68 side is established in the pressure chamber 60, and the closure valve 104 and the circulating pump 106 are formed in this collection pipe way 102. The tip part of the collection pipe way 102 has immersed into the application-of-pressure water 65 in the application-of-pressure tank 68. That is, if the closure valve 84 is opened, and the bypass valve 82 is closed and the circulating pump 106 is driven, the inside of the pressure chamber 60 is decompressed and the pressure chamber 60, each pipeline 66, the air bubbles adhering to the wall of 102 grades, etc. can be discharged to the application-of-pressure tank 68 side. It is possible to return it to the application-of-pressure tank 68 through the collection pipe way 102, supplying the application-of-pressure water 65 of this pressure chamber 60 to the pressure chamber 60 through the feed water pipe line 66 from the application-of-pressure tank 68 by the simultaneous drive of the pumps 80 and 106, and to also make it circulate between the application-of-pressure tanks 68.

[0074]While the heater 108, the temperature sensor 110, the pressure sensor 112, and the sound generator 114 are formed in the wall surface section of the pressure chamber 60 and heating of the application-of-pressure water 65 accommodated, and its temperature or pressure is detected, Sound waves, such as an ultrasonic wave, can be added to the pressure chamber 60 from the sound generator 114 if needed.

[0075]And the pressurizing piston 116 is formed in the pressure chamber 60 as a force means, enabling a free attitude, The pressurizing piston 116 is supported by the support cylinder part 117 which made the wall surface section of the pressure chamber 60 project, and is closed between the support cylinder part 117 and the pressurizing piston 116 with O ring 119 which is a sealing means. The actuator 120 and the motor 122 are attached to this pressurizing piston 116 as a

pressurizing driving means via the spring 118 for application of pressure. The motor 122 comprises a stepping motor, and rotation of this motor 122 is changed into forward/backward moving by the actuator 120, and is added to the spring 118 for application of pressure by it, The pressure in the pressure chamber 60 can be made to fluctuate according to the attitude of the pressurizing piston 116, at the time of penetration of the pressurizing piston 116, at the time of retreat of high voltage and the pressurizing piston 116, low pressure is produced and the pressure variation gives an application-of-pressure stimulus to the cell 5 on the scaffold 7 through the pressure-receiving film 64. The position of the pressurizing piston 116 is detected by the position sensing device 123, and the detected information is used for control of an attitude of the pressurizing piston 116, i.e., control of an application-of-pressure stimulus.

[0076]In this case, the pressure which the pressure chamber 60 is filled up with the application-of-pressure water 65, and is applied from the pressurizing piston 116, It acts on the pressure-receiving film 64 extensively through the application-of-pressure water 65, and the pressure can make hydrostatic pressure able to act on the cell 5 or tissue uniformly through the culture medium 3 from the pressure-receiving film 64, and can make a strain (displacement) act uniformly similarly. And the dynamic range of a pressure change amount can be enlarged in control of the movement magnitude of the pressurizing piston 116, and control fine from a small value to a big value is possible. And when it is detected by the position sensing device 123, and is supervised by the control device 40 and the movement magnitude arrives at a limit position, movement of the pressurizing piston 116. An alarm output can be emitted from the control device 40 as the culture apparatus 1 being unusual, and an alarm display can be carried out to the displaying means (display 232 grade of drawing 5) connected to the control device 40, or an administrator can be notified through communication lines, such as a telephone.

[0077]The liquid-sending device 12 which sends the culture medium 3 to the culture chamber 20 continuously or intermittently equips the in-and-out side with the liquid-sending chamber 128 which has the sending-area check valve 124 and the suction side check valve 126, and is removably attached to the culture warehouse 42 with the screw 130. While the liquid-sending piston 132 is attached to the liquid-sending chamber 128, enabling a free attitude and the sterilization liquid pool 134 is formed in the halfway part of this liquid-sending piston 132, the spring 136 for application of pressure is attached. Between the liquid-sending piston 132 and the body part of the liquid-sending chamber 128, O rings 133 and 135 which are sealing means are formed. The sterilization liquid pool 134 was filled up with antibiotics, such as a germicide, an antibacterial, or penicillin, and invasion of the biomass from the outside or a foreign matter is prevented to it. The spring 136 for application of pressure is accommodated in the caddis 137.

[0078]The actuator 138 and the motor 140 are attached to the rear end part of the liquid-sending piston 132 as a driving means. The motor 140 comprises a stepping motor, and rotation of this motor 140 is changed into forward/backward moving by the actuator 138, and is added to the spring 136 for application of pressure by it, According to the attitude of the liquid-sending piston 132, the pressure in the liquid-sending chamber 128 fluctuates, and the pressure variation is applied to the valve elements 142 and 144 of each check valves 124 and 126. If the liquid-

sending piston 132 is pulled out from the liquid-sending chamber 128, while the inside of the liquid-sending chamber 128 will become negative pressure by the cash drawer of the liquid-sending piston 132, the valve element 142 will be reduced by the stability of the spring 143 and the sending-area check valve 124 will close, When the valve element 144 can pull up against the welding pressure of the spring 145 and the suction side check valve 126 opens, the culture medium 3 is sucked in in the liquid-sending chamber 128. Since the inside of the liquid-sending chamber 128 will be pressurized, the valve element 144 will descend, the suction side check valve 126 will close, the valve element 142 will go up and the sending-area check valve 124 will open if the liquid-sending piston 132 advances into the liquid-sending chamber 128, The culture medium 3 in the liquid-sending chamber 128 is sent out to the culture chamber 20 side.

[0079]The pressure buffer 18 of the culture medium 3 is provided with the pressure relief valve 26, and the pressure relief valve 26 is removably attached to the culture warehouse 42 with the screw 146. This pressure relief valve 26 moves to the valve chest 148, the valve element 150 which can be opened and closed is attached, and the sterilization liquid pool 153 is formed in the halfway part of the plunger 152 of this valve element 150. Between the plunger 152 and the body part of the valve chest 148, O rings 155 and 157 which are sealing means are formed. The sterilization liquid pool 153 was filled up with antibiotics, such as a germicide, an antibacterial, or penicillin, and invasion of the biomass from the outside or a foreign matter is prevented to it. The actuator 156 and the motor 158 as a driving means are attached to the rear end part of the plunger 152 of the valve element 150 via the buffer spring 154. The motor 158 comprises a stepping motor and, as for the operating pressure which rotation of this motor 158 is changed into forward/backward moving, is applied to the buffer spring 154, and opens the valve element 150 with the actuator 156, is adjusted according to the degree of compaction of the buffer spring 154. That is, when the degree of compaction of the buffer spring 154 is high, the pressure from the culture medium 3 required in order to open the valve element 150 becomes high, and when the degree of compaction of the buffer spring 154 is low, the pressure from the culture medium 3 required in order to open the valve element 150 becomes low. Such a pressure buffer 18 is formed because the welding pressure applied to the culture medium 3 of the culture chamber 20 is buffered by the culture circuit unit 4 side.

[0080]The suction tube 164 is branched and formed in the tube 50D which connects the valve chest 148 and the culture medium bag 48 of this pressure relief valve 26 with the pinch valve 162, The pinch valve 166, the check valve 168, and the culture liquid pool 170 are formed in this suction tube 164, and the culture liquid pool 170 is connected with the collection pipe way 102 through the suction tube 165. The pinch valve 162 opens and closes the tube 50D, and the pinch valve 166 is used for opening and closing of the suction tube 164. When the valve element 169 is made to stop with the welding pressure of the spring 171 and the pressure of the culture medium 3 exceeds the welding pressure of the spring 171, the culture medium 3 flows through the check valve 168 into the culture liquid pool 170 side through the suction tube 164. The pinch valve 166 can stop the suction tube 164 by the operation independently [the check valve 168], and can prevent the conduction of the culture medium 3 by the stoppage. Since the culture liquid pool 170

is a well-closed container and the inside of the culture liquid pool 170 will be decompressed if the closure valve 104 is closed and the circulating pump 106 is driven when the pinch valve 166 is open, The valve element 169 can be moved against the welding pressure of the spring 171, the check valve 168 can be opened, and the culture medium 3 can be drawn in the culture liquid pool 170 side at this time.

[0081]The N_2 gas bomb 172, the O_2 gas bomb 174, and the CO_2 gas bomb 176 are connected with the culture warehouse 42 through the pipelines 178, 180, and 182, respectively as gas mixture and the concentration adjustment 36, The gas switching valves 184, 186, and 188, the flow control valves 190, 192, and 194, the flow meters 196, 198, and 200, the pressure regulators 202, 204, and 206, and the valves 208, 210, and 212 are installed in each pipelines 178, 180, and 182. That is, 1 of N_2, O_2, or CO_2 or 2 or more are supplied and mixed by opening and closing the gas switching valves 184-188 selectively.

[0082]While the humidification service-water saucer 216 and the fan 218 for stirring which are humidification means and which collect the humidification service water 214 as humidity control devices 32 are installed in the culture warehouse 42, The heater 220 for gas heating, the temperature-inside sensor 222, and the fan 218 for stirring are installed as the thermostat 34 which is a heating method. The fan 218 for stirring is driven with the fan motor 224.

[0083]Although reference is made [emitting warning and] at the time of the abnormal occurrence of the culture apparatus 1, since the cell 5 and tissue under culture are saved regardless of the classification of abnormalities until an administrator performs required treatment, the control device 40 continues the insulation control in the culture warehouse 42, control of gas concentration, and liquid-sending operation. Such continuous operation makes the insulation control in the culture warehouse 42, control of gas concentration, and liquid-sending operation continue similarly, also when operation is normally completed even if predetermined culture time comes and.

[0084]Next, drawing 5 shows the example of composition of the manual operating device 38 and the control device 40. The manual operating device 38 and the control device 40 are provided with the main control unit 230 which comprised a personal computer etc. The external storages 234, such as the displays 232, such as a display and a liquid crystal, a hard disk, an optical disc, a floppy disk, and an IC card, and the input device 236 of the keyboard are connected to the main control unit 230. The input device 236 constitutes some or all of the manual operating device 38.

[0085]In the main control unit 230, through the temperature detector 238, the detect output of the temperature sensor 110, Through the temperature detector 240, through the detect output of the temperature-inside sensor 222, and the pressure detection circuit 242 The detect output of the pressure sensor 112, The detect output of the position sensing device 123 and the detecting output of the detection switch 54 are applied, In the driving output of the drive circuit 248 and the heater 108, the driving output of the drive circuit 250, the valves 184 and 186, and the valve 188 The drive circuit 252, [the driving output of the motor 122] [the driving output of the drive circuit 244 and the motor 140] [the driving output of the drive circuit 246 and the motor 158] While

the driving output of the drive circuit 254 and the heater 220 is obtained for the driving output of the fan motor 224 from the drive circuit 256, the driving output of the sound generator 114 is obtained.

[0086]Next, the cell of this invention or the culturing method of an organization is explained with reference to the operation flow chart shown in drawing 6.

[0087]Step S1 is the initialization mode. The process with which this initialization mode fills the application-of-pressure water 65 in the pressure chamber 60 after wearing of the culture circuit unit 4, and the culture medium 3 is filled in the culture circuit unit 4, The process of sampling and carrying out the hold stores of the operation amount of the pressure impression device 16 of the culture pressurizer 8 equivalent to the pressure value by which the setting input was carried out, and the pressure buffer 18 is included. The operation amounts for obtaining a setting pressure with the air bubbles etc. which the paces of expansion of the construction material which constitutes the culture circuit unit 4 and the pressure-receiving film 64 differ, and remain in the pressure chamber 60 differ. So, these preset values are corrected in the initialization mode.

[0088]If equipped with the culture circuit unit 4, gas mixture and the concentration adjustment 36, the humidity control device 32, and the thermostat 34 are operated, and while filling up the inside of the culture warehouse 42 with gas, it will control to moderate moisture and optimal temperature. And the application-of-pressure water 65 which opens the feed water valve 92 and becomes the application-of-pressure tank 68 from a waterworks etc. is filled up to setting water level, the bypass valve 82 and the closure valves 84 and 104 are opened, the pump 80 is operated, and the application-of-pressure water 65 is supplied in the pressure chamber 60. When it is detected with the flowing water sensor 70 and the application-of-pressure water 65 of the specified quantity is detected, the amount of supply of the application-of-pressure water 65 to the pressure chamber 60 suspends the pump 80, and switches it to the circulating movement by the circulating pump 106.

[0089]In circulating movement, the bypass valve 82 is closed and it switches to the channel to the by-pass line 88. At this time, the amount of conduction of the application-of-pressure water 65 is restricted by the orifice 86, the inside of the pressure chamber 60 serves as negative pressure with the suction force of the circulating pump 106, and the air bubbles which remain in the pressure chamber 60 are discharged at the application-of-pressure tank 68 side. At this time, the pinch valve 162 is closed, the pinch valve 166 is opened, and the culture chamber 20 is filled up with the culture medium 3 in the culture medium bag 48 through the tubes 50E, 50A, and 50B with the negative pressure produced with the circulating pump 106. After carrying out predetermined time operation of the circulating pump 106 and making the culture chamber 20 fill up with the culture medium 3, the pinch valve 166 is closed, the pinch valve 162 and the bypass valve 82 are opened, and the negative pressure by circulating flow is canceled, and the circulating pump 106 is stopped. Then, after closing the closure valves 84 and 104, temperature control is started by heating the application-of-pressure water 65 in the pressure chamber 60 with the heater 108, and detecting the temperature with the temperature sensor 110.

[0090]Next, the motor 158 of the pressure buffer 18 is operated, the pressure relief valve 26 is

closed, and the tube 50C is made to blockade with constant pressure. The pressure impression device 16 is operated until the maximum pressure Pmax which operated the motor 122 and set it up beforehand is detected. When the maximum pressure Pmax is detected, the pulse count of the motor 122 is memorized in the memory of the main control unit 230. Next, the motor 158 of the pressure buffer 18 is rotated until the present pressure value declines, and the pulse count of the motor 158 is memorized for this pressure value in the memory of the main control unit 230 as a position of the maximum pressure Pmax.

[0091]Next, it is made to rotate until the minimum pressure Pmin which set up the motor 122 of the pressure impression device 16 beforehand is detected. When the minimum pressure Pmin is detected, the pulse count of the motor 122 is memorized in the memory of the main control unit 230. Next, the motor 158 of the pressure buffer 18 is rotated, the motor 158 is suspended in the position which starts reduction from the minimum pressure Pmin, and the pulse count value of this motor 158 is then memorized in the memory of the main control unit 230.

[0092]Next, it shifts to Step S2 after this initialization mode, and it is judged whether it is pressure variable culture mode. That is, when shifting to the pressure variable culture mode of Step S3 when it is judged whether it cultivates by changing a pressure periodically and it performs a pressure variable, and cultivating by a constant pressure, it shifts to the fixed pressure power culture mode of Step S7.

[0093]In the pressure variable culture mode of Step S3, application of pressure, pressure maintenance, decompression, and pressure maintenance are repeated to every cycle T, and the application-of-pressure stimulus of the cell 5 of the culture chamber 20 is carried out, and the culture medium 3 is sent.

[0094]In step S4, it is judged whether the error of the pressure by operation of the pressure impression device 16 and the pressure buffer 18, and Pmax and Pmin is beyond a predetermined value. When the error beyond a predetermined value arises, the movement magnitude of the pressure impression device 16 which shifts to Step S5 and is in agreement with each value of the maximum pressure Pmax and the minimum pressure Pmin, and the pressure buffer 18 is sampled, and the memory value of the memory of the main control unit 230 is corrected.

[0095]Next, in Step S6, when Step S3 - Step S6 are repeated and the predetermined culture time t passes until the predetermined culture time t passes, it is considered as the end of culture and shifts to Step S11.

[0096]In the fixed pressure power culture mode of Step S7, the cell 5 or tissue is stimulated with a fixed pressure, and the culture medium 3 is sent. That is, at Step S8, it is judged whether the error of the pressure and the setting pressure Ps by operation of the pressure impression device 16 and the pressure buffer 18 is beyond a predetermined value. When the error beyond a predetermined value arises, the movement magnitude of the pressure impression device 16 which shifts to step S9 and is in agreement with the setting pressure Ps, and the pressure buffer 18 is sampled, and the memory value of the memory of the main control unit 230 is corrected. And in Step S10, when the predetermined culture time t passes, it is considered as the end of culture and shifts to Step S11.

[0097]Next, at Step S11, the living body cell preservation mode of operation is performed. It is necessary to save the cell 5 thru/or tissue healthfully until it starts the transfer for transplantation, even if culture of the cell 5 or tissue is generated [completion, i.e., an organization,]. In the living body cell preservation mode of operation, maintaining the cell 5 to prescribed temperature, the culture medium 3 is supplied and a living body cell is held in the healthy state.
[0098]Next, at Step S12, it judges whether the shutdown command was inputted for transplantation of the organization which consists a living body cell of being transplantation 5, i. e., a cell, and circulation of the culture medium 3 and temperature control are suspended with a shutdown command. The culture circuit unit 4 is desorbed and the cell 5 thru/or tissue are transported with the culture circuit unit 4.
[0099]Next, drawing 7, drawing 8, and drawing 9 show the setting input operation in the initialization mode, the numerals a, b, and c, d, and e are the connectors of the flow chart divided and indicated, and coincidence of numerals a-e is a bond part.
[0100]At Step S21, the culture the culture under periodic application of pressure or under a constant pressure is inputted for the culture chamber 20. In Step S22, when making a pressure change periodically, it shifts to Step S24 and displays "a pressure variable." When cultivating under a constant pressure, it shifts to Step S23 and "pressure regularity" is displayed.
[0101]In Step S25, the cycle T into which a pressure is made to change is inputted. It judges whether it is within the limits which can perform the cycle T inputted at Step S26, and it displays and notifies of "reinput of the cycle T" at the time besides a real line range, and it reinputs by shifting to Step S27 and shifting to Step S25. If it is in a real line range, display of the "cycle T" shifted and set as Step S28 and memory to the memory of the main control unit 230 will be performed.
[0102]At Step S29, retention time t_1 of the maximum pressure Pmax is inputted. At Step S30, it is judged whether inputted time t_1 is in the working range of the cycle T. If it is outside a working range, it will notify by the display of "reinput of t_1" and will reinput by shifting to Step S31 and shifting to Step S29. If it is in a working range, it will shift to Step S32 and display of "maximum pressure retention time t_1" and memory to the memory of the main control unit 230 will be performed.
[0103]At Step S33, retention time t_2 of the minimum pressure Pmin is inputted. At Step S34, it is judged whether inputted time t_2 is in the working range of the cycle T. If it is outside a working range, "reinput of t_2" will be displayed and it will reinput by shifting to Step S35 and shifting to Step S33. If it is in a working range, it will shift to Step S36 and display of "minimum pressure retention time t_2" and memory to the memory of the main control unit 230 will be performed.
[0104]At Step S37, difference time of time (t_1+t_2) is considered as the inputted cycle T for 2 minutes, and application of pressure and decompression time t_3 are calculated. At Step S38, it is

judged whether time t_3 is in a working range. When it is outside a working range, it judges that the value of the cycle T, time t_1, and t_2 is not suitable, and returns to Step S25. When time t_3 is in a working range, calculated time t_3 is stored in the memory of the main control unit 230, and "application of pressure and decompression time t_3" are displayed in Step S39. At Step S40, it is inputted whether change of lenience and severity is attached at the time of application of pressure and decompression. When attaching lenience and severity in Step S41, it shifts to Step S42, and when not attaching lenience and severity, it shifts to Step S46. At Step S42, the input of the variation for attaching lenience and severity at the time of application of pressure and decompression is performed. At Step S43, it is judged whether the inputted variation can operate. When operation is impossible, it reinputs by shifting to Step S44, displaying "reinput of application of pressure and decompression variation", and shifting to Step S42. If operation is possible, it will shift to Step S45 and display of "application of pressure and the amount of decompression" and memory to the memory of the main control unit 230 will be performed. The simulation screen of pressure displacement may be displayed at this time.

[0105]The minimum pressure Pmin is inputted at Step S46. At Step S47, it is judged whether it is within limits which can perform the pressure impression device 16. If it is outside a real line range, it will shift to Step S48, "reinput of the minimum pressure Pmin" will be displayed, and reinput will be performed at Step S46. If it is in a real line range, it will shift to Step S49 and display of "the minimum pressure Pmin" and memory to the memory of the main control unit 230 will be performed.

[0106]At Step S50, the maximum pressure Pmax is inputted and it is judged in Step S51 whether it is within limits which can perform the pressure impression device 16. If it is outside a real line range, it will shift to Step S52, "reinput of the maximum pressure Pmax" will be displayed, and reinput will be performed at Step S50. If it is in a real line range, it will shift to Step S53 and display of "the maximum pressure Pmax" and memory to the memory of the main control unit 230 will be performed.

[0107]At Step S54, the controlling temperature ct of the pressure chamber 60 is inputted. It is judged at Step S55 whether it is within limits which can be performed. If it is outside a real line range, it will shift to Step S56, "reinput of the temperature ct" will be displayed, and it will reinput at Step S54. If it is in a real line range, it will shift to Step S57 and display of "the temperature ct" and memory to the memory of the main control unit 230 will be performed.

[0108]At Step S58, the circulating flowing quantity f of the culture medium 3 of the culture circuit unit 4 is inputted. It is judged at Step S59 whether it is within limits which can be performed. If it is outside a real line range, it will shift to Step S60, and it displays and notifies of "reinput of the circulating flowing quantity f", and reinputs at Step S58. If it is in a real line range, it will shift to Step S61 and display of "the circulating flowing quantity f" and memory to the memory of the main control unit 230 will be performed.

[0109]Operation time is inputted at Step S62. At Step S63, display of "operation time" and memory to the memory of the main control unit 230 are performed.

[0110]If a relation with the pressure applied to the pressurizing piston 116 in the pressure impression device 16, the cell 5, or tissue here is explained, When A (cm^2) and a pressure are set to P (kg/cm^2) and power is set to F (kgf), the cross-section area of the pressurizing piston 116 the power F. If it becomes F=PxA, and the load rate of the spring 118 for application of pressure is set to K (kgf/mm) and the spring shrinkage amount is made into L_2 (mm), since it is $F=KxL_2$, the power F is $KxL_2=PxAL_2=(PxA)/K$... (1)

It becomes. That is, when the pressurizing piston 116 moves, the elastic force of the spring 118 for application of pressure acts on the pressurizing piston 116, and the pressurizing piston 116 compresses the application-of-pressure water 65 in the pressure chamber 60. By being compressed, in the pressure chamber 60, a pressure rises and the pressure is detected with the pressure sensor 112. Displacement of this pressurizing piston 116, i.e., the relation between movement magnitude (mm) and the pressure P (kg/cm^2), becomes like drawing 10, for example. In drawing 10, the movement magnitude by the motor 122 and L_2 L_1 The shrinkage amount of the spring 118 for application of pressure, The movement magnitude of the pressurizing piston 116 in case L_3 does not use the spring 118 for application of pressure, The movement magnitude of the pressurizing piston 116 by contraction of the air which is mixing L_4, the movement magnitude of the pressurizing piston 116 according [L_5] to contraction of water, and L_6 show the movement magnitude of the pressurizing piston 116 by modification of the container of the culture chamber 20 and the pressure chamber 60. L_3 is total of L_4, L_5, and L_6 and L_1 expresses total of L_2 and L_3. The relation of the movement magnitude of the pressurizing piston 116 by this pressure impression device 16 and the pressure value of the pressure sensor 112 is stored in the memory of the main control unit 230.

[0111]setting capacity (at the time of application of pressure) of V (cm^3) and air to Va (cm^3) for the capacity (1-atmosphere o'clock) of air, if the movement magnitude of the pressurizing piston 116 by contraction of air is explained -- 1xV=(Pa+1) xVa =, if it is fixed, As for the capacity Va of air, movement magnitude L_4 (mm) of the pressurizing piston 116 become Va =V/(Pa+1) and according to contraction of air is $L_4=10x\{(V-Va)/A\}$.

$=[\{V-V/(Pa+1)\}/A]\ x10$ ... (2)

It becomes.

[0112]The movement magnitude of the pressurizing piston 116 by compression of water and the culture medium 3 is as follows. Namely, if the compression ratio (40degreeC) of W (cm^3) and water is made into $0.44x10^{-5}$ (cm^2/kg), the volume of water and the culture medium 3, Compression amount deltaW (cm^3) of water and the culture medium 3, Movement magnitude L_5 (mm) of the pressurizing piston 116 become $deltaW=0.44x10^{-5}xPxW$ and according to compression of water and the culture medium 3 is $L_5=deltaW/Ax10=10x\{(0.44x10^{-5}xPxW)/$

A}.
... (3)
It becomes. Movement magnitude L_6 of the pressurizing piston 116 by modification of a container since shrinkage amount deltaWt is deltaWt =WxCt when contraction of the appearance by modification of the pressure vessel 22 and the culture vessel 61 is set to Ct here is L_6= (deltaWt /A) x10=10x {(WxCt) /A}.
... (4)
It becomes. Therefore, the total movement magnitude of the pressurizing piston 116 serves as value L_1 adding a formula (1), (2), (3), and (4).

[0113]In the pressure buffer 18 side, if the pressure applied to the buffer spring 154 is reduced, the pressure in the culture chamber 20 will overcome the pressure concerning the pressure relief valve 26, the pressure relief valve 26 will open, the culture medium 3 will pass the pressure relief valve 26, and the pressure by the side of the culture chamber 20 will decline. It settles down in the place where the welding pressure of the buffer spring 154 and the pressure by the side of the culture medium 3 balanced. If power which balances the blocking surface product by the pressure relief valve 26 with B (cm^2), and balances a pressure with P (kg/cm^2) and the pressure P when the power applied to the pressure relief valve 26 of the pressure buffer 18 is explained is set to F (kgf), When it becomes F=PxB and the amount of shrinkage of K (kgf/mm) and the buffer spring 154 is set to m (mm) for the load rate of the buffer spring 154, the balancing power F serves as F=Kxm and the amount m of shrinkage of the buffer spring 154 is expressed by m=PxB/K. Drawing 11 shows the relation of the pressure applied to the pressure relief valve 26 side, i.e., the pressure which acts on the movement magnitude (the amount of shrinkage of the buffer spring 154) and the pressure relief valve 26 by the side of the actuator 156, i.e., adjustment discipline. In drawing 11, m_1 shows the case where m_2 uses two springs which are different to the buffer spring 154, when the single buffer spring 154 is used.
[0114]Since the capacity of the liquid-sending device 12 is small, most of contraction of the culture medium 3, modification of a container, gaseous contraction, etc. can be disregarded. Therefore, since the amount V (ml) of liquid sending of the liquid-sending piston 132 is V=Cxl when it is made into the cross-section area C of the liquid-sending piston 132 (cm^2), and the movement magnitude l (cm), the movement magnitude l serves as l=V/C and movement magnitude determines it according to the amount of liquid sending. When there is much movement magnitude of the liquid-sending piston 132 of the liquid-sending device 12, return to the original position immediately after movement of the liquid-sending piston 132, but. When there is little movement magnitude of the culture medium 3, it does not return, but at the time of the next liquid-sending operation, if the liquid-sending piston 132 is further moved from the position and it moves to the position which cannot move, it will return to the original position. At this time, when it becomes higher than the acceptable value of the descent pressure of setting out, it is necessary to amend the data of the movement magnitude of the actuator 156 of the pressure

relief valve 26, and the relation of a pressure memorized before operation based on this value.
[0115]Next, drawing 12 expresses the execution gestalt in the pressure variable culture mode performed at Step S3 of drawing 6. Namely, drawing 12 is a timing chart showing the pressure condition impressed to the culture chamber 20, and application-of-pressure timing, Pressure transition of the culture chamber 20 and (b) show the operation timing of the pressure buffer 18, (c) shows the application-of-pressure timing of the pressure impression device 16, and, as for (a), (d) shows the liquid-sending timing of the culture medium feed unit 6.
[0116]Application of pressure and decompression are repeated [culture chamber 20] between the maximum pressure Pmax and the minimum pressure Pmin the cycle T. t_1 is time to hold the maximum pressure Pmax, and t_2 is time to hold the minimum pressure Pmin. t_3 is the operating time at the time of application of pressure and decompression. These maximum pressures Pmax, the minimum pressure Pmin, time t_1, t_2, and t_3 can be arbitrarily changed according to the part in the living body which carries out external culture. It can also decompress by choosing and pressurizing a suitable numerical value with the data of a living body's age in the cell 5 which should be cultured, sex, height, weight, a part in the living body, etc.
[0117]Before the pressure buffer 18 starts application of pressure, it is operated to the position which can obtain the maximum pressure Pmax with the maximum speed by time t_5, and blockades the tube 50C. Then, operation of the pressure impression device 16 is started through the time delay of t_4, and it pressurizes from the minimum pressure Pmin to the maximum pressure Pmax at the speed equivalent to time t_3.

[0118]After holding by time t_1 of the maximum pressure Pmax, the pressure impression device 16 operates again and starts decompression from the maximum pressure Pmax to the minimum pressure Pmin at the speed equivalent to time t_3. After the pressure impression device 16 operates, only time t_6 is delayed, only the time t_7 operates and the pressure buffer 18 cancels the blocking power of the tube 50C.
[0119]When pressure control is started, it is made to increase from the pressure 0 neighborhood to the maximum pressure Pmax. At this time, the pressure buffer 18 moves to a blockade position with maximum velocity, the pressure impression device 16 is operated after time t_9 progress, and application of pressure between time t_8 until it reaches the maximum pressure Pmax at the speed equivalent to time t_3 is performed.

[0120]After being held at the minimum pressure Pmin, after progress of time t_{11}, only the time t_{12} operates and the culture medium feed unit 6 sends out the culture medium 3 to the culture chamber 20. The amount of liquid sending can be arbitrarily set up by changing time t_{12}. The liquid-sending piston 132 is retreated after liquid sending between time t_{14} in which only time t_{13}

is almost equal to time t_{12} after progress. Although the liquid was sent by retention time t_2 of the minimum pressure Pmin in this example, the liquid may be sent by retention time t_1 of the maximum pressure Pmax or application of pressure, and decompression time t_3.

[0121]Next, drawing 13 expresses other execution gestalten in the pressure variable culture mode performed at Step S3 of drawing 6. Namely, drawing 13 is a timing chart showing the pressure condition impressed to the culture chamber 20, and application-of-pressure timing, (a) shows the modification of the pressure pattern which (c) impresses pressure transition of the culture chamber 20, and (b) to the operation timing of the pressure buffer 18, impresses it to the application-of-pressure timing of the pressure impression device 16, and impresses (d) to the liquid-sending timing 20 of the culture medium feed unit 6, i.e., a culture chamber.

[0122]In this example, the pressure pattern applied, for example to the cartilage of the knee at the time of a walk is reproducible by sending out the pressure impression pattern which fluctuated ram speed and the secondary decompression speed to application of pressure and decompression time t_3 functionally, and attached lenience and severity to them, and attaching lenience and severity to pressure fluctuation. In this case, as the pressure impression device 16 is shown in time t_{15}, t_{16}, and t_{17}, working speed is changed, and in time t_3, lenience and severity are added to welding pressure. Since other operations are the same as operation of drawing 12, the explanation is omitted.

[0123]Next, drawing 14 thru/or drawing 21 show a 2nd embodiment of the cell of this invention, or the culture apparatus of an organization, As for drawing 14, the side side arrangement of a culture apparatus and drawing 16 the transverse-plane side arrangement of a culture apparatus, and drawing 15 The important section of a culture apparatus, The important section of the culture apparatus drawing 17 removed the culture circuit unit 4, and excluding [drawing 18] the culture circuit unit 4 and drawing 19 show the pressure impression device 16, drawing 20 shows the culture medium feed unit 6, and drawing 21 shows the pressure buffer 18. Identical codes are given to the 1st embodiment and identical parts.

[0124]This culture apparatus is constituted by the single housing 260, and the housing 260 is divided in the culture chamber 262, the machinery room 264, and control and a power source room 266. Although the culture warehouse 42 is accommodated in the inside of the culture chamber 262 and the composition in the culture warehouse 42 is the same as that of a 1st embodiment, a different point comprises the treating part 268 with single culture medium feed unit 6, pressure impression device 16, and pressure buffer 18 grade.

[0125]The doors 270 and 272 opened and closed independently are formed in the culture chamber 262 and the machinery room 264, The application-of-pressure tank 68 grade is accommodated in the machinery room 264 with the working part of the culture medium feed unit 6, the pressure impression device 16, and the pressure buffer 18, and each actuators 120, 138, and 156 are supported with the common tie-down plate 269 at the back side of the machinery room

264, as shown in drawing 15. The water supply opening 274 and the exhaust port 276 are formed in the wall surface of the machinery room 264. The control device 40 and the electric power unit are accommodated in control and the power source room 266, and the electric power switch 278 is installed in the front panel side with the display 232.

[0126]Next, as shown in drawing 16, the culture warehouse 42 is accommodated in the culture chamber 262, and the culture circuit unit 4 and the treating part 268 are accommodated in the culture warehouse 42. As shown in drawing 17 and drawing 18, the handling unit 280 by the side of the culture circuit unit 4 is constituted removable by the treating part 268.

[0127]Next, drawing 19 shows the pressure impression device 16 containing the culture vessel 61 which constitutes the culture chamber 20, and the pressure vessel 22. In this case, the actuator 120 of the pressure impression device 16 attaches the ball screw 284 to the housing 282, and combines the motor 122 with the rear end part of this ball screw 284 at the coupling joint 286. The movable bed 288 which carries out longitudinal slide movement to the ball screw 284 by rotation is formed, and the two springs 118A and 118B for application of pressure polymerized between this movable bed 288 and the backup flange 290 provided in the front end part side of the ball screw 284 are installed. That is, a compression state changes with ****** DDO 288 which the springs 118A and 118B for application of pressure move according to rotation of the ball screw 284, and the elasticity of each springs 118A and 118B for application of pressure acts on the pressurizing piston 116 side. It may replace with the ball screw 284 and the actuator 120 may consist of a belt, a cam, etc.

[0128]Next, drawing 20 shows the culture medium feed unit 6. The actuator 138 attaches the ball screw 292 to the housing 291, and combines the motor 140 with the rear end part of this ball screw 292 at the coupling joint 294. The movable bed 296 which carries out longitudinal slide movement to the ball screw 292 by rotation is formed, and the rear end part of the liquid-sending piston 132 touches the front part of the piston hand plate 298 attached to this movable bed 296. Namely, when ****** DDO 296 which moves according to rotation of the ball screw 292 by the motor 140 moves forward, If the spring 136 for application of pressure is compressed, when the liquid-sending piston 132 moves forward and ****** DDO 296 goes astern, compression of the spring 136 for application of pressure will be solved, and the liquid-sending piston 132 will retreat according to the returning force of the spring 136 for application of pressure. The culture medium 3 can be sent out by the attitude of the liquid-sending piston 132.

[0129]Next, drawing 21 shows the pressure buffer 18. The actuator 156 attaches the ball screw 302 to the housing 300, and combines the motor 158 with the rear end part of this ball screw 302 at the coupling joint 304. The movable bed 306 which carries out longitudinal slide movement to the ball screw 302 by rotation is formed, The plunger hand plate 308 is attached to this movable bed 306 via the polymerized buffer springs 154A and 154B, and the rear end part of the plunger 152 of the pressure relief valve 26 touches the front part of this plunger hand plate 308. That is, when ****** DDO 306 which moves according to rotation of the ball screw 302 by the motor 158 moves forward, the plunger hand plate 308 is advanced with the buffer springs 154A and 154B, and the compression state of the buffer springs 154A and 154B changes. That is, the valve

element 150 is forced via the buffer springs 154A and 154B in a compression state, and the pressure relief valve 26 is held at a state of obstruction. This holding state changes with rotation of the ball screw 302, and the compression states of the buffer springs 154A and 154B accompanying it.

[0130]Next, drawing 22 shows the modification of the culture medium feed unit 6. Although the spring 136 for application of pressure was installed in the liquid-sending piston 132 in the culture medium feed unit 6 shown in drawing 2, drawing 3, and drawing 14, The connection shaft 310 is attached to the movable bed 296 which moves by the ball screw 292 of the actuator 138 except for the spring 136 for application of pressure, and it may be made to connect the rear end part of the liquid-sending piston 132 at the tip of this connection shaft 310 by the fixing means of lock-pin 312 grade. Even if constituted in this way, the liquid-sending piston 132 can be made to move by the right inversion of the ball screw 292.

[0131]Next, drawing 23 shows a 3rd embodiment of the cell of this invention, or the culture apparatus of an organization. As arrow Pr shows from the compressor which is not illustrated in this embodiment inside the pressure chamber 60 formed with the pressure vessel 22 of the pressure impression device 16, Application-of-pressure air is made to act through the pipeline 67 provided with the pressure regulator 314, the pressure-up valve 316, and the needle valve 318, The application-of-pressure air in the pressure chamber 60 is made to discharge through the collection pipe way 102 provided with the needle valve 320 and the pressure-lowering valve 322, It may replace with the tube 50D side at the valve 11 (drawing 1) or the pinch valve 162 (drawing 2), and the valve 323 opened and closed by rotation of the actuator 321 may be formed. An application-of-pressure stimulus can be added to the cell 5 by using together the operation which makes the valve 323 blockade intermittently, and the operation which makes application-of-pressure air act and pressurizes the pressure-receiving film 64. In this case, in order to give change to an application-of-pressure stimulus, the opening and closing control of the pressure-up valve 316 and the pressure-lowering valve 322 can perform. When such air is used, while being able to enlarge the pressure change amount per unit movement in high voltage, with low pressure, small the pressure change amount per unit movement, When impressing a pressure to a cell or tissue, it becomes absorbable [an unnecessary vibration generated from a motor, an actuator etc.], and the accuracy of the application-of-pressure stimulus to a cell or tissue can be raised.

[0132]Next, drawing 24 and drawing 25 show a 4th embodiment of the cell of this invention, or the culture apparatus of an organization. The cell 5 which should be cultured is transplanted to the scaffold 7 fabricated from collagen etc., and is stored in the culture chamber 20 every scaffold 7. The culture medium 3 is supplied to the culture chamber 20 through the culture circuit unit 4 from the culture medium tub 49. The culture circuit unit 4 constitutes the closed circuit, and the pump 324, the pressure sensor 326, and the pressure buffer 18 as the liquid-sending device 12 are formed in this culture circuit unit 4. The detection pressure power of the pressure sensor 326 is applied to the pressure controller 328, and the control output according to the detection pressure power is applied to the pump 324 from the pressure controller 328. That is, the pressure P of the

culture medium 3 is controlled uniformly.

[0133]The buffer spring 154 is placed between the plungers 152 of the valve element 150 of the pressure relief valve 26 inserted in some culture circuit units 4 by the pressure buffer 18, it attaches the actuator 156, and connects the motor 158 with this actuator 156. Rotation of the motor 158, i.e., normal rotation, an inversion, a stop, and revolving speed are controlled by the control device 40. That is, rotation of the motor 158 is transmitted to the ball screw 302, and the movable bed 306 moves forward and backward according to the hand of cut by rotation of the ball screw 302. Since this movement is transmitted to the plunger 152 of the valve element 150 via the buffer spring 154, the closing force of the valve element 150 is set up by the position of the movable bed 306, and the compressive force of the buffer spring 154. When the pressure of the culture medium 3 with the pump 324 overcomes the closing force of the valve element 150, the valve element 150 is opened and the culture medium 3 passes the pressure relief valve 26.

[0134]And the air pipe way 330 which takes in gas, such as oxygen or carbon dioxide, is established in the culture medium tub 49, and the filter 332 which prevents invasion of saprophytic bacteria, a foreign matter, etc. is formed in the air pipe way 330. That is, oxygen or carbon dioxide taken in from the air pipe way 330 is transmitted to the cell 5 of the culture chamber 20 with the culture medium 3.

[0135]According to such composition, by driving the pump 324, the culture circuit unit 4 is supplied, and the culture medium 3 carries out conduction to the culture chamber 20, and supplies gas, such as nourishment required for the cell 5, oxygen, or carbon dioxide. By driving the pressure buffer 18, the culture circuit unit 4 is blockaded and the pressure in the culture chamber 20 rises with the pressure applied to the culture medium 3 from the pump 324. The arbitrary pressure values which balance the pressure applied from the pump 324 by adjustment of the cushioning power of the pressure buffer 18, i.e., the closing force of the valve element 150, can be acquired.

[0136]Drawing 25 shows this pressurizing operation. By operating the pressure buffer 18 periodically, the maximum pressure Pmax and the minimum pressure Pmin can be given to the cell 5 by turns. That is, time t_1 is set up for the maximum pressure Pmax, time t_2, pressure-up time t_3, and pressure-lowering time t_3 are set to the cell 5 for the minimum pressure Pmin, pressure circulation of the culture medium 3 is obtained like a living body, and growing environment equivalent to a living body is realized. And by controlling the working speed of the pressure buffer 18, time t_1, t_2, and t_3 can be adjusted arbitrarily and the optimum state according to the characteristic and the living body part of the cell 5 to cultivate can be realized.

[0137]

[Effect of the Invention]According to this invention, the following effect is acquired as explained above.

It can cultivate efficiently, without being polluted with the bottom of the environment imitating a environment in the living body, and the cell or tissue near inside-of-the-body tissue which is moreover easy to unite with inside-of-the-body tissue can be cultivated.

b By holding the cell or tissue of a living body in a specific culture position, setting up under the environment imitating a living body, supplying culture medium continuously or intermittently, and applying continuation, an intermission, or the pressure that changes periodically, It is close to the ideal and practical organization corresponding to the living body's part which should be restored, i.e., inside-of-the-body tissue, and culture of inside-of-the-body tissue and the organization which is easy to unite can be realized.
The cell or tissue in which c culture should do can be held in the state of floating or un-floating in culture medium, and efficient culture can be performed in the state where it was stabilized extremely.
Since d cell or tissue is held by hydro-gell or a scaffold by a floating state in culture medium, culture of a cell or tissue can be promoted.
Since what was constituted including two or more substances or all that was chosen from one or these of various amino acid, sugars, salts, or protein having corresponded to the cell or tissue which should cultivate e culture medium is used, efficient culture, and a quality cell or tissue can be cultivated.
Since f culturing environment is added to the physiological condition of a living body's part, or this physiological condition and it sets up according to the characteristic data for every living body of age, height, weight, sex, and others, the cell or tissue which is easy to unite with inside-of-the-body tissue can be cultivated.
Since living body environment is set up by setting out and control of supply of gas, such as g nitrogen, oxygen, or carbon dioxide, and control, temperature, or humidity, climate control near a living body can be realized and it can contribute to culture of the cell which is moreover easy to unite with inside-of-the-body tissue or tissue near inside-of-the-body tissue.
By applying a pressure corresponding to a living body's part which h restoration should carry out, an ideal and practical cell or tissue can be formed.
By making the pattern of i pressure into continuation, an intermission, or the gestalt that changes periodically, and choosing or combining it, ideal physical irritation can be realized, the metabolism of a cell, the concentration gradient of a division cycle and a living thing stimulus, and distribution can be affected, and promotion of culture can be aimed at.
Since j culture units supply culture medium required for the cell or tissue which accommodated the cell or tissue which should cultivate in the culture chamber, and was intercepted with the open air, the open air, the intercepted cell, or tissue is protected from contamination of a biomass etc., and, as a result, can cultivate a quality organization. Since a desired pressure is given by the force means in addition to the physical irritation by the hydrostatic pressure by culture medium, and a flow, a cell or the tissue can receive influence in the concentration gradient of the metabolism of a cell, a division cycle, and a living thing stimulus, or distribution, and can promote culture of a cell or tissue. Since the supplying form of a cell or the culture medium to an organization is set up arbitrarily and can be supplied intermittently or continuously by a culture medium feeding means, promotion of culture can be aimed at by physical irritation with a variation.
By being able to control arbitrarily k force means or a culture medium feeding means, and using

the control means of a computer etc., While copying living body environment by performing various kinds of programmed control, such as feedback control and feed-forward control, desired environment can be set up and efficient culture can be performed.
How, i.e., a pressure pattern, to apply l pressure can perform more efficient culture by setting up corresponding to the cell or tissue which should cultivate.
m pressure pattern can be set as all gestalten, and can perform culture of a cell or tissue efficiently by the selection and combination.
n culture culture units provided with the culture chamber which accommodates the cell or tissue which did, A cell or tissue can be independently moved [main part / of a culture apparatus] with separation and the culture units separated from the open air since it was removable, during movement, a cell or tissue can be protected from contamination by a biomass etc., and reliability, such as a living body's restoration, can be improved.
While setting out of the culturing environment by supply of desired gas is attained by intercepting a closed space which is o culture spaces with the open air, a cell or tissue can be protected from contamination by the open air.
While supplying gas, such as nitrogen, oxygen, or carbon dioxide, to the culture units accommodated in p closed space, by equipping culture units with a gas-absorption means, gas can be given to a cell or tissue and living body environment can be copied by supply and control of gas.
By making the culture spaces formed of q closed space fill up with gas, such as nitrogen, oxygen, or carbon dioxide, living body environment can be copied and desired culture spaces can be formed.
It has a culture medium tub for supplying or circulating culture medium required for r culture units, and since a culture medium tub is moreover installed in the open air and the intercepted closed space, the pollution control of culture medium can be planned.
While being able to give an application-of-pressure stimulus in the state where it intercepted with the open air by installation of s pressure-receiving film to the cell or tissue accommodated in the culture chamber, an application-of-pressure stimulus of the request of the stimulus imitating living body environment, etc. is realizable.
If the pressure regulation is performed by a pressure buffering means when some t culture units are pressurized, physical irritation near living body environment can be realized, and promotion of culture of a cell or tissue can be aimed at.
As means forming of u pressure, even if it uses any of water pressure, oil pressure, or pneumatic pressure, a desired application-of-pressure stimulus can be realized, and living body environment can be copied with sufficient accuracy.
If constituted from a liquid-sending device which pressurizes and sends out the culture medium which incorporated v culture medium feeding means into the liquid-sending chamber, culture units can be made to supply or circulate through culture medium efficiently, and the desired amount of liquid sending can be set up by controlling this pressurizing amount.
Since the pressure applied to w culture medium is buffered, can give a cell or tissue an ideal

application-of-pressure stimulus, for example, the pressure of culture medium using a pressure relief valve by control of a pressure relief valve. It can control to an ideal pressure condition, without making culture medium pollute, if a pressure relief valve is opened and the pressure of culture medium is dropped.
The temperature and humidity of a closed space in which x culture units are accommodated can be controlled, and the culture spaces corresponding to living body environment can be formed.
y living body has received the acoustical stimulus from the external world, can copy living body environment acoustically by using a sound generator together, when he moreover pours in the cell or tissue which should cultivate to a culture chamber, can use an ultrasonic wave together and can also perform efficient and reliable pouring.
By controlling the gas concentration supplied to z closed space by a control means, living body environment can be copied and it can contribute to a cell or the promotion of culture of an organization.

CLAIMS

[Claim(s)]
[Claim 1]A cell holding a cell or tissue of a living body in a specific culture position, supplying culture medium to said cell or said tissue while setting up said cell or said tissue under environment imitating a living body, and cultivating said cell or said tissue in said culture position, or a culturing method of an organization.
[Claim 2]While setting up said cell or said tissue under environment which held a cell or tissue of a living body in a specific culture position, and copied a living body and supplying culture medium to said cell or said tissue continuously or intermittently through a culture circuit, A cell applying to said cell or said tissue continuation, an intermission, or a pressure that changes periodically, and cultivating said cell or said tissue in said culture position, or a culturing method of an organization.
[Claim 3]The cell according to claim 1 or 2 provided with holding mechanism which makes said cell which should be cultured in said culture position, or said tissue hold by floating state or a non-floating state in said culture medium, or a culturing method of an organization.
[Claim 4]The cell according to claim 1 or 2 using a scaffold absorbed by said cell or said tissue with the growth while holding hydro-gell which makes said cell or said tissue hold by a floating state in said culture medium to said holding mechanism, said cell, or said tissue, or a culturing method of an organization.
[Claim 5]The cell according to claim 1 or 2 constituting said culture medium including 1 of various amino acid, sugars, salts, or protein, or 2 or more, or a culturing method of an organization.
[Claim 6]The cell according to claim 1 or 2, wherein said environment where said cell or said tissue is cultivated is set up according to characteristic data for said every living body of age, height, weight, sex, and others in addition to a physiological condition of said living body's part,

or this physiological condition, or a culturing method of an organization.
[Claim 7]The cell according to claim 1 or 2, wherein said environment is set up with gas, such as nitrogen, oxygen, or carbon dioxide, temperature, or humidity supplied through said culture medium, or a culturing method of an organization.
[Claim 8]The cell according to claim 2 setting up arbitrarily said pressure applied to said cell or said tissue according to said cell or said part of said organization, or a culturing method of an organization.
[Claim 9]The cell according to claim 2, wherein said pressure applied to said cell or said tissue is a pressure which consists of continuation, an intermission, pressures that change periodically, or these combination, or a culturing method of an organization.
[Claim 10]A cell or a culture apparatus of an organization characterized by comprising the following.
Culture units which are provided with a culture chamber which accommodates a cell or tissue, and supply culture medium.
A force means which gives said cell or said tissue in said culture chamber a pressure, and a culture medium feeding means to which said culture units are made to supply said culture medium intermittently or continuously.

[Claim 11]The cell according to claim 10 provided with a control means which controls said force means or said culture medium feeding means, or a culture apparatus of an organization.
[Claim 12]The cell according to claim 10 setting up arbitrarily said pressure applied to said cell or said tissue according to said cell or said tissue from said force means, or a culture apparatus of an organization.
[Claim 13]The cell according to claim 10 or a culture apparatus of an organization with which said pressure applied to said cell or said tissue from said force means is repeatedly characterized by a thing which were followed for every intermittence state and fixed time, and which is made to fluctuate for every fixed time.
[Claim 14]The cell according to claim 10 being disengageable independently from a main part of a culture apparatus in said culture units, or a culture apparatus of an organization.
[Claim 15]The cell according to claim 10 which accommodates said culture units in the open air and an intercepted closed space, and is characterized by things, or a culture apparatus of an organization.
[Claim 16]The cell according to claim 10 provided with a gas-absorption means which can absorb gas, such as nitrogen, oxygen, or carbon dioxide, or a culture apparatus of an organization.
[Claim 17]The cell according to claim 10 making it come to fill up said closed space gas, such as nitrogen, oxygen, or carbon dioxide, or a culture apparatus of an organization.
[Claim 18]The cell according to claim 10 provided with a culture medium tub which collects said culture medium which should be supplied to said culture units, or a culture apparatus of an organization.
[Claim 19]The cell according to claim 10 provided with a pressure-receiving film pressured from

the exterior to said culture chamber, or a culture apparatus of an organization.
[Claim 20]The cell according to claim 10 equipping said culture units with a pressure buffering means, or a culture apparatus of an organization.
[Claim 21]The cell according to claim 10 attaching a pressure chamber to said culture chamber via said pressure-receiving film, making water pressure, oil pressure, or pneumatic pressure act on this pressure chamber, and applying a pressure to said cell or said tissue in said culture chamber, or a culture apparatus of an organization.
[Claim 22]The cell according to claim 10 constituting said culture medium feeding means from a liquid-sending device which pressurizes and sends out said culture medium which provided a liquid-sending chamber in said culture units, and was incorporated into this liquid-sending chamber, or a culture apparatus of an organization.
[Claim 23]The cell according to claim 10 installing a pressure relief valve in said culture units, opening said pressure relief valve when a pressure of said culture medium exceeds a constant pressure arbitrarily set as said pressure relief valve, and dropping a pressure of said culture medium, or a culture apparatus of an organization.
[Claim 24]The cell according to claim 10, wherein a heating method or a humidification means is installed and said closed space is maintained and controlled by a desired temperature or humidity, or a culture apparatus of an organization.
[Claim 25]The cell according to claim 10 provided with a sound generator which gives sound waves, such as an ultrasonic wave, to said culture chamber of said culture units, or a culture apparatus of an organization.
[Claim 26]The cell according to claim 10 which is provided with a control means which controls gas concentration supplied to said closed space, and is characterized by things, or a culture apparatus of an organization.

[Translation done.]